

39957

## REMARKS

### Entry of Amendment

As Applicants are filing a RCE herewith, this amendment should be entered and considered by the Examiner at this time.

Applicants have the following comments in support of this amendment and in response to the Final Rejection of July 24, 2008.

### Claim Amendments

The claimed pharmaceutical compositions of the present application are directed to formulations of a new and novel highly-halogenated halogenated xanthene that is fully substituted with iodine and bromine atoms (i.e., disodium 4,5,6,7-Tetrabromoerythrosin) and which the inventors of the present application were the first to have conceived. The inventors have further created a chemotherapeutic pharmaceutical composition consisting of this novel halogenated xanthene.

As explained herein, while Applicants traverse the rejections in the Final Rejection, in order to advance prosecution of the present application, Applicants are amending Claims 1, 10, 36 and 37, and canceling Claims 9 and 11 (without prejudice or disclaimer). Independent Claims 1, 36 and 37 have been amended to clarify the claimed invention and to specify that the claimed injectable composition is formulated of a disodium salt of 4,5,6,7-Tetrabromoerythrosin (i.e., as disclosed in Table 1 of the specification of the present application as filed). The claimed indication for such compositions has been amended to recite the preferred embodiment of the invention described in

Applicants' specification, specifically compositions adapted to chemotherapeutic treatment of cancer. Hence, no new matter has been added. Therefore, it is respectfully requested that these amendments be entered and allowed.

As explained below, the pending claims are in an allowable condition, and it is respectfully requested that they be allowed.

Applicants will now specifically address each of the Examiner's objections and rejections in the order in which they appear in the Final Rejection.

#### Drawing

In the Final Rejection, the Examiner is requiring new corrected drawings "because Figs. 1a and 1b are structurally incorrect see the 112, 2<sup>nd</sup> rejection below."

In order to advance the prosecution of this application, Applicants are amending Figs. 1a and 1b and submitting corrected drawings, as discussed in more detail below in the discussion of the §112, 2<sup>nd</sup> paragraph rejection. The structures in these corrected drawings are chemically correct and supported by the specification of the present application.

Accordingly, it is respectfully submitted that this objection has been overcome, and it is requested that the objection be withdrawn.

#### Claim Rejections – 35 USC §112, Second Paragraph

The Examiner also rejects Claims 1, 9-11, 36 and 37 under 35 USC §112, second paragraph, as being indefinite. A number of reasons for this rejection are enumerated in the Final Rejection.

Each of these is respectfully traversed, for at least the reasons discussed in the following sections.

Functionalities at positions R<sup>1</sup> and R<sup>2</sup>. The Examiner objects to Claims 1 and 36-37 and the claim language “wherein the functionalities at positions R<sup>1</sup> and R<sup>2</sup> each comprise an element selected from the group consisting of sodium, potassium and hydrogen” therein as being indefinite as “the claims do not recite any formulas for 4,5,6,7-Tetrabromoerythrosine which comprise an R<sup>1</sup> and R<sup>2</sup> substituent.” This objection is respectfully traversed.

While Applicants traverse this objection, in order to advance prosecution of this application, independent Claims 1, 36 and 37 have been amended to recite that only the disodium form of 4,5,6,7-Tetrabromoerythrosin (i.e., as disclosed in Table 1 of the specification as filed, R<sup>1</sup> and R<sup>2</sup> are each sodium) is claimed, and have deleted the objected to language “wherein the functionalities at positions R<sup>1</sup> and R<sup>2</sup> each comprise an element selected from the group consisting of sodium, potassium and hydrogen.” Applicants respectfully submit that this claim language specifically reciting the claimed halogenated xanthene in the disodium form overcomes this objection. Accordingly, it is respectfully requested that this objection be withdrawn.

Structural representation in Figures 1a and 1b. The Examiner also objects to certain irregularities in Figures 1a and 1b. In order to advance the prosecution of this application, Applicants are amending Figures 1a and 1b so as to be structurally correct with the structure of the halogenated xanthenes disclosed in the specification and claims of the present application. No new matter has been added in the amendments to these figures. Further, as noted above, Claims 1, 36 and 37 have been amended to clarify the halogenated xanthene being claimed. It is respectfully submitted that these amendments overcome the Examiner’s objection, and it is requested that this objection be withdrawn.

Accordingly, it is respectfully submitted that each of the objections in the 35 USC §112, second paragraph rejection have been overcome, and it is requested that the rejection be withdrawn.

Claim Rejections - 35 USC §112, First Paragraph

The Examiner also rejects Claim 10 under 35 USC §112, first paragraph, for lack of enablement. This rejection is also respectfully traversed.

While Applicants traverse this rejection, in order to advance the prosecution of this application, Applicants are amending Claim 10 to recite the features of “wherein said pharmaceutical composition is for the treatment of cancer of the skin, the mouth and digestive tract, the urinary and reproductive tracts, the respiratory tract, the head and neck, and the endocrine and lymphoreticular systems.” It is also noted that independent Claim 1 has been amended to recite “wherein said pharmaceutical composition is adapted for chemotherapeutic treatment of cancer.” Applicants believe that these amendments should overcome the Examiner’s concerns about this claim, regarding the breadth of the claim vs the disclosure of the specification.

In further support of Claim 10 and Applicants’ other pending claims, Applicants are providing the following additional information. In furtherance of Applicants’ conceptions and inventions, Applicants have conducted a series of studies on these halogenated xanthenes as part of a development program for human oncology applications. These studies have demonstrated that certain formulations of the halogenated xanthenes have broad spectrum anti-neoplastic utility against a wide variety of tumors. For example, the following table outlines experiments demonstrating successful ablation of homograft, xenograft, and spontaneous tumors in mice with halogenated xanthenes. These tumors include murine melanomas, human and murine breast carcinomas, murine

hepatocellular carcinomas, and human multidrug resistant small cell lung and prostate carcinomas.

**Tumor Response of Various Tumor Cell Lines to a Single Intralesional (IL) Dose of PV-10 (10% Rose Bengal Disodium in Saline)**

<b>Species</b>	<b>Tumor Cell Line</b>	<b>Results</b>
C57BL/6 Mice	Murine B16/F10	Tumor response and necrosis observed in all treated tumors. Regrowth of tumor was observed in the margins after eleven days.
BALB/c Nude Mice 4/group	Human Breast Carcinomas: MCF-7 [ER+] MCF-7 [ER-] HTB-133 T47-D [ER-]	IL PV-10 completely ablated MCF-7 [ER+] (4/4), MCF-7 [ER-] (4/4), and HTB-133 (4/4) tumors within 21 days. Most long Passage T-47D [ER-] tumors were ablated (3/4).
Neu+/+ x (1988A2Kb x Neu++)	Spontaneous Murine Breast Carcinoma	IL PV-10 ablated spontaneous breast tumors in mice.
BALB/c Nude Mice 8/group	Murine Hepa I-6 Hepatocellular Carcinoma	IL PV-10 completely ablated all tumors (8/8) with no damage to peripheral normal tissue (0/8)
Nu/nu Nude Mice	H69Ar Human Multidrug Resistant Small Cell Lung Carcinoma	IL PV-10 fully ablated 5/5 tumors 24 hours post injection and over 7 days of observation.
Nu/nu Nude Mice	PC-3 Human Prostate Carcinoma	IL PV-10 fully ablated 8/8 tumors 24 hours post injection and over 29 days of observation.

In addition, Applicants have shown ablation of spontaneous tumors with halogenated xanthenes in a number of companion animals, including:

- Canine recurrent fibrous histiocytoma
- Canine mast cell
- Canine bladder
- Equine melanoma
- Equine sarcoid
- Feline squamous epithelial

In furtherance of these results, Applicants have compared the pharmacologic properties of 4,5,6,7-Tetrabromoerythrosin vs Rose Bengal (0.01% formulations of the disodium salts of each molecule) for ablation of murine renal adenocarcinoma (ATCC CCL-142 RAG) in the BALB/c nude mouse, and found that the two halogenated xanthenes exhibit similar antineoplastic activity.

Accordingly, Applicants have shown that medicaments formed from the claimed halogenated xanthenes have clear potential for broad spectrum antineoplastic use.

It is respectfully submitted that as these examples demonstrate, and in light of the disclosure in the specification, undue experimentation is not required to practice the medicaments of amended Claim 10 or the other claimed subject matter.

Therefore, Claim 10 and the other claims of the present application are sufficient enabled, and it is respectfully requested that this rejection be withdrawn.

#### Interview Request

If the Examiner still wishes to reject the claims of the present application after considering this amendment, then Applicants request a telephone interview with the Examiner to discuss the rejections in further depth. In such a case, it is respectfully requested that the Examiner contact the undersigned to set-up such an interview prior to the issuance of a further Office Action for this application.

#### Conclusion

It is respectfully submitted that the claims of the present application are in an allowable

condition and should be allowed.

If any further fee should be due for this amendment, the extension of time, and/or RCE, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

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Fig. 1a

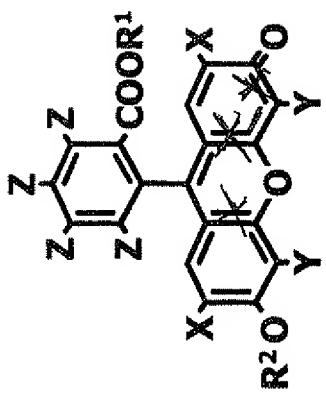


Fig. 1b

